Heterocyclic Imines and Amines. Part 19.[1] Isoquinoline and Other Products from α,o-Dicyanostilbene and Basic Reagents

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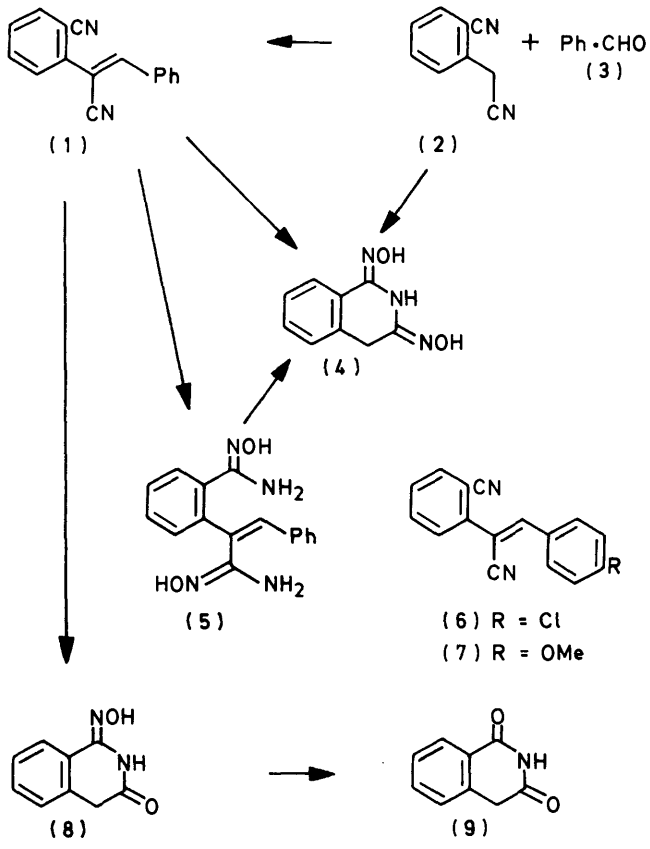
α,o-Dicyanostilbene (1) was cleaved by hydrazine or hydroxylamine under mildly acid conditions to o-cyanobenzyl cyanide (2) and benzaldehyde, isolated as derivatives. Sodamide with compound (1) gave 1-amino-4-cyano-3-phenylisoquinoline: alkoxides similarly gave the 1-alkoxy compounds, the presumed intermediate 3,4-dihydroisoquinoline from the methoxide reaction being isolated and separately dehydrogenated. Acid hydrolysis of the 1-ethoxy compound gave the known 4-cyano-3-phenylisoquinolin-1(2*H*)-one. With the anion of o-cyanobenzyl cyanide, compound (1) gave a 1-amino-4-cyano-3-(2-substituted phenyl)isoquinoline, which was oxidised to 1-amino-4-cyano-3-(2-carboxyphenyl)isoquinoline. The latter lost water at 210 °C to give yellow 12-cyano-5-iminoisoindolo[2,1-*b*]isoquinolin-7(5*H*)-one, closely related to known compounds.

Many 1,2- and 1,3-dicyano compounds add basic reagents to form heterocyclic products.[2] In continuing studies in this field, we have examined the behaviour of α,o-dicyanostilbene (1) towards hydrazine, hydroxylamine, sodamide, sodium ethoxide, and the anion of o-cyanobenzyl cyanide: isoquinoline products arise. The starting 1,3-dicyanide (1) is readily accessible[3] through Knoevenagel condensation of benzaldehyde with o-cyanobenzyl cyanide (2).

Reactions with Hydrazine and Hydroxylamine.—The dicyanide (1) was recovered almost completely after being heated with hydrazine hydrochloride in ethanol. (Reaction with the base is reserved for a separate publication.) From reaction with a mixture of hydrazine hydrochloride and hydrazine in boiling aqueous ethanol, some dicyanide (1) was recovered (21%): products obtained were o-cyanobenzyl cyanide (35%) and benzaldehyde azine (31%). Clearly the reaction conditions were tending to reverse the original condensation (2) + (3) ⟶ (1). It was not then surprising that compound (1) with a mixture of hydroxylamine and its hydrochloride under similar conditions afforded homophthalimide dioxime[4] (4), derived from (2) which in turn arose from (1). Attempts to isolate benzaldehyde oxime as a second product were unsuccessful. However, when the chloro analogue (6) was treated with hydroxylamine and its hydrochloride analogously, p-chlorobenzaldehyde oxime was isolated as well as the cyclic dioxime (4).

When the dicyanide (1) was heated with hydroxylamine itself in aqueous ethanol, the bis(amide oxime) (5) resulted. This was unexpectedly stable and unlike glutaric bis(amide oxime)[5] failed to cyclise even at 200 °C and 0.5 mmHg. The bis(amide oxime) (5) also resisted boiling aqueous ethanolic sodium carbonate, but with hydroxylamine hydrochloride in boiling ethanol yielded the known homophthalimide dioxime (4), the cyclisation being accompanied or preceded by hydrolytic removal of the benzaldehyde residue in compound (5). From a further experiment in which the dinitrile (5) was heated with a mixture of hydroxylamine and its hydrochloride in aqueous ethanol, the homophthalimide monoxime (8) was obtained (decomp. 230 °C), clearly isomeric with the monoxime, m.p. 158 °C, which Eichelbaum[6] had obtained from o-cyanobenzyl cyanide (2) and 1 molar proportion of hydroxylamine. The new mono-oxime structure (8) was supported by the ready hydrolysis to homophthalimide (9) and by the chemical shift of the 8-proton, *peri* to the 1-oximino group, which was almost the same as that in homophthalimide dioxime (4) (Table 1).



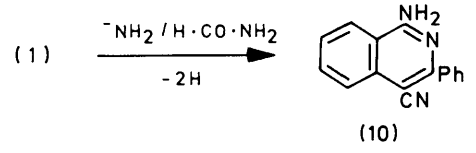
Reaction with Sodamide.—With sodamide in formamide the dicyano compound (1) yielded a product $C_{16}H_{11}N_3$ corresponding to addition of NH_3 and loss of 2 H. There was no analogy with the behaviour of other 1,3-dicyano compounds[5,7,8] or o-cyanocinnamonitrile.[9] The product had a u.v. absorption rather similar to those of the authenticated isoquinolines listed in Table 2, but with the longest wavelength band shifted bathochromically, consistent with an aminoisoquinoline structure. The presence of an amino group was indeed confirmed by the two-proton signal at δ 5.85 in the ^{1}H n.m.r. spectrum (which went on deuteriation), and by the i.r. absorption. The latter also showed a sharp line at 2 193

Table 1. ^{1}H N.m.r. results for homophthalimide and oximes in $(CD_3)_2SO$ containing $SiMe_4$

Compound	Chemical shifts (δ)				
	4-CH_2	8-H	NH	1-NOH	3-NOH
Homophthalimide (9)	4.02	8.04	11.2		
Monoxime (7)	3.84	7.85	9.62	10.94	
Dioxime (4)	3.79	7.83	8.59	10.70	10.02

Table 2. U.v. absorption maxima for 1-alkoxy-4-cyano-3-phenylisoquinolines in 96% ethanol

Compound (11; Ar = Ph) R	$\lambda_{max.}$/nm (ε × 10^{-3})				
Me	217 (30.8)	256 (29.0)	308 (13.4)	325sh (10.4)	337sh (6.0)
Et	217 (34.3)	256 (33.2)	309 (16.0)	325sh (12.6)	339sh (6.9)
Pr	217 (32.4)	256 (31.0)	309 (14.6)	325sh (11.8)	339sh (6.2)
Bu	217 (31.4)	256 (30.3)	309 (14.5)	325sh (11.5)	340sh (6.1)

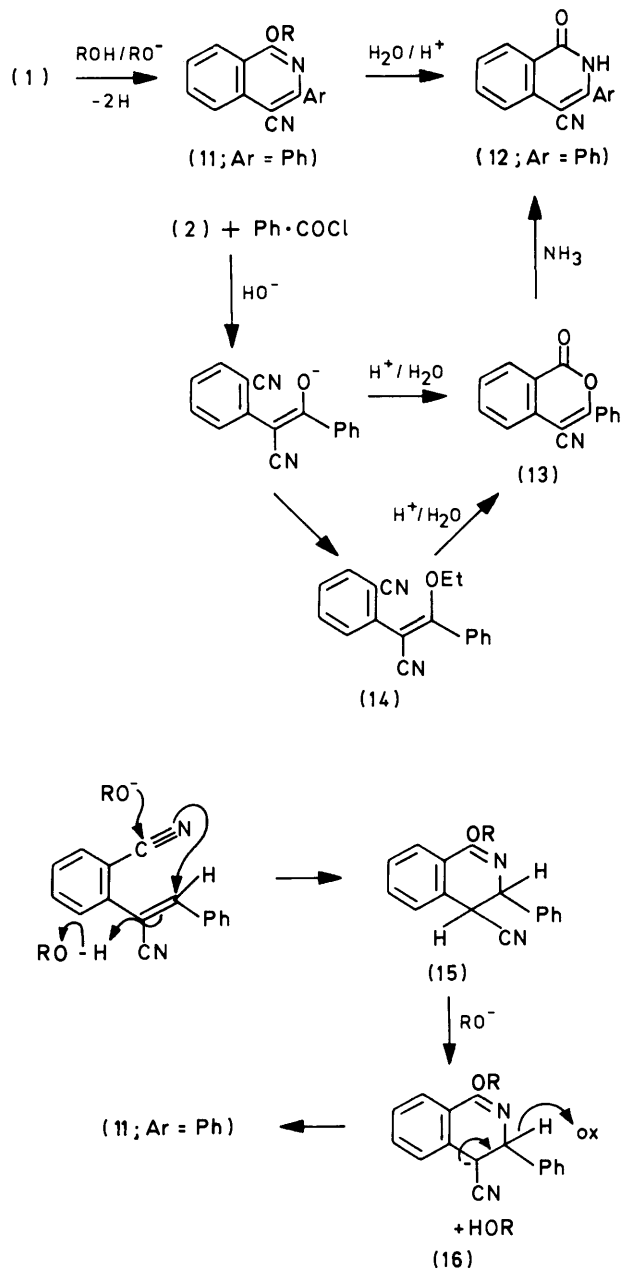


(10)

cm^{-1} from a cyano group conjugated to an amino function.[1] These facts and possible reaction mechanisms lead to the 1-amino-4-cyano-3-phenylisoquinoline structure (10). Despite very stringent precautions to exclude oxygen, the presumed intermediate dihydroisoquinoline was not isolated (*vide infra*).

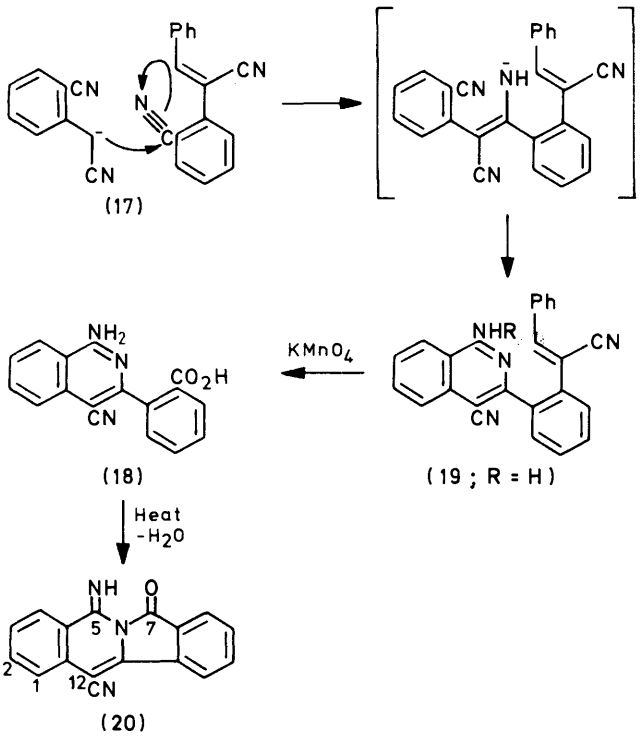
Reactions with Alkoxides.—Treatment of α,*o*-dicyanostilbene (1) with ethanolic sodium ethoxide yielded a product $C_{18}H_{14}N_2O$, formally derived by addition of ethanol to the alkene (1) followed by dehydrogenation. Corresponding products $C_{16}H_9N_2(OR)$ were obtained using sodium methoxide, propoxide, and butoxide (but not isopropoxide), each in the corresponding alcohol. These products showed a single cyano group absorption in the i.r. spectrum at *ca.* 2 220 cm^{-1} and broad maxima in the u.v. spectrum at 256 and 309 nm with the absorption extending out to 360 nm, which suggested [1] that cyclisation to an isoquinoline structure had occurred. Consideration of possible mechanisms led to structure (11). This was confirmed for the ethoxy compound (11; R = Et, Ar = Ph) by acid hydrolysis to the isoquinolin-1(2*H*)-one (12; Ar = Ph) and comparison with an authentic sample prepared by Gabriel and Newmann's method,[10] from the isocoumarin (13) and ammonia. Furthermore, the ethoxystilbene (14), isomeric with the isoquinoline (11; R = Et, Ar = Ph), was also obtained and shown to be distinct. The isocoumarin (13) and stilbene (14) were prepared [11] by *C*-benzoylation of *o*-cyanobenzyl cyanide (2) followed, respectively, by acid cyclisation, and by ethylation of the silver enolate. Acid treatment of the ethoxystilbene (14) also provided the isocoumarin (13).

Probably, the 1-cyano-4-alkoxyisoquinolines (11) arose through initial attack of alkoxide upon the aryl cyano group of the dicyanostilbene (1) (see Scheme), followed by cyclo-



Scheme.

addition of the imino anion onto the stilbene double bond to give 3,4-dihydroisoquinolines (15) as primary products. Dehydrogenation to (11) had obviously occurred under the conditions employed, so further experiments were performed with exclusion of air. Sodium methoxide in methanol then yielded a mixture, shown by mass spectrometery and ^{1}H n.m.r. to comprise *ca.* 70% of the dihydroisoquinoline (15; R = Me) with 30% of the aromatised product (11; R = Me, Ar = Ph). When the dihydro compound (15; R = Me) had been separated and purified, it proved to be stable to air and was unchanged when refluxed in methanol under oxygen. However, in the presence of methoxide, dehydrogenation by oxygen occurred. Possibly, the alkoxide gives rise to the dihydroisoquinoline anion (16) which then parts with hydride to oxygen or an oxygen derived acceptor (see Scheme). Circumstances did not permit further experimentation, unfortunately, but it did appear from the slowness of the dehydrogenation of



the dihydroisoquinoline (15; R = Me) with oxygen and alkali that oxygen itself was probably not the primary hydride acceptor under the original conditions in which the isoquinolines (11) arose. Perhaps the oxidant is a peroxy compound derived from the stilbene (1) and oxygen, which would not have been present in the model dehydrogenation experiments.

That the cyclisation–dehydrogenation reactions with alkoxides (and sodamide) were not unique to the dicyanostilbene (1) was shown by the analogous behaviour of the *p*-methoxy analogue (7) with methoxide in methanol to yield 4-cyano-1-methoxy-3-(4-methoxyphenyl)isoquinoline (11; R = Me, Ar = *p*-C_6H_4OMe). This last, with hot aqueous acid, yielded the corresponding isoquinolin-1(2*H*)-one (12; Ar = *p*-C_6H_4OMe).

Reaction with o-*Cyanobenzyl Cyanide.*—Although *o*-cyanobenzyl cyanide (2) undergoes self-addition in the presence of alkali,[1] it adds surprisingly efficiently to some other cyano compounds, *e.g.* *o*-cyanotoluene.[12] This encouraged us to examine the addition of *o*-cyanobenzyl cyanide (2) to α,*o*-dicyanostilbene (1). When equimolar amounts of these two cyanides were kept at 60 °C in methanol containing sodium methoxide, a new product $C_{25}H_{16}N_4$ was isolated, together with some 4-cyano-1-methoxy-3-phenylisoquinoline (11; R = Me, Ar = Ph) from the action of methoxide on (1). The new product showed u.v. maxima at 220, 255, and 305 nm with two shoulders at longer wavelengths, reminiscent of 3-phenylisoquinolines (Table 2). The high resolution i.r. spectrum showed two cyano groups with characteristically low wave numbers,[1] and the presence of a primary amino function. This latter group was confirmed by the two-proton signal in the ^1H n.m.r. spectrum (in MeCN) at δ 6.46 which was eliminated on shaking the deuteriochloroform solution with deuterium oxide. The rest of the n.m.r. spectrum, comprising a fourteen-proton envelope signal at δ 7.2—8.2, was unchanged. Evidently, the methylene group of the *o*-cyanobenzyl cyanide component had taken part in the addition to the α,*o*-dicyanostilbene (1), such that neither proton was retained on the original carbon atom. Examination of the likely modes of addition of *o*-cyanobenzyl cyanide anion (17) to (1) followed by intramolecular cylisation of the resulting *N*-anionic species (and protonation) leads to a set of six tentative structures for the new product (neglecting structures with 4-membered rings). Of these six, only structure (19) adequately accommodates the physical data. Support came from oxidation experiments. Following ozonolysis of the *N*-acetyl derivative (19; R = Ac) and reductive work-up, benzaldehyde was isolated (as its dinitrophenylhydrazone) in reasonable yield, whilst after treatment of the suspected compound (19) with permanganate a hygroscopic compound $C_{17}H_{11}N_3O_2$ was isolated, for which the amino acid structure (18) was consistent with its properties. The i.r. spectrum of (18) showed a sharp absorption at 2 216 cm^{-1} from a single cyano group, a broadened NH_2 absorption, and a carboxyl carbonyl band at 1 660 cm^{-1}. When heated to 210 °C, the amino acid (18) lost water, giving the expected γ-lactam $C_{17}H_9N_3O$, with structure (20), as indicated by the sharp i.r. absorption for imine, cyano, and γ-lactam carbonyl groups, and the yellow colour characteristic also of the related 12-phenylisoindolo[2,1-*b*]isoquinol-7(5*H*)-one and -5,7-dione.[13]

A methoxy analogue of the isoquinoline (19) was obtained by addition of *o*-cyanobenzyl cyanide to the dicyanostilbene (7) in the presence of methoxide, indicating that the foregoing preparation of the isoquinoline (19) could be extended.

Experimental

U.v. data were from solutions in 96% ethanol, obtained with a Unicam SP 800 B spectrophotometer. I.r. maxima were from spectra recorded for Nujol mulls with either a Grubb-Parsons Spectromaster or a Unicam SP 200 instrument. ^1H N.m.r. spectra were recorded at 60 MHz and 35 °C with a Perkin-Elmer R12 spectrometer, using solutions in $(CD_3)_2SO$ containing $SiMe_4$ as internal reference. Ether refers to diethyl ether throughout.

Reactions of α,o-*Dicyanostilbene* (1).—(*a*) *With hydrazine.* (i) The dicyanide[3] (1) was recovered (98%) after a solution [1.73 g of (1) in ethanol (100 ml)] had been refluxed with hydrazine dihydrochloride (7.88 g) in water (30 ml) for 24 h. (ii) The dicyanide (1) (1.73 g) in ethanol (100 ml) was refluxed with hydrazine hydrate (0.75 g) and hydrazine dihydrochloride (1.61 g) in water (40 ml) for 28 h. Cooling the solution at 0 °C gave the dicyanide (1) (0.37 g, 21%) with correct m.p. 125 °C and i.r. spectrum, $\nu_{max.}$ 2 223 (aryl CN), 2 212 (αβ-unsat. CN), 1 595 cm^{-1} *etc.* Evaporation of the filtrate to 40 ml, filtration through charcoal and cooling gave *o*-cyanobenzyl cyanide (0.3 g, 35%), m.p. and mixed m.p. 77 °C.[7,14] Water was added to the filtrate until turbid: the solid was collected, dried, dissolved in benzene and chromatographed on alumina (50 g; 100—200 mesh) to afford yellow prisms (0.38 g, 31%), m.p. 92 °C (lit.,[15] 93 °C), *m/z* 208, of benzalazine.

(*b*) *With hydroxylamine.* (i) The dicyanide (1) (1.15 g, 0.005 mol) in ethanol (40 ml) was refluxed with hydroxylamine hydrochloride (1.39 g, 0.02 mol) and sodium hydrogen carbonate (0.84 g, 0.01 mol) in water (15 ml) for 3 h. Cooling and evaporation (under reduced pressure) gave 1,3-bishydroxyimino-1,2,3,4-tetrahydroisoquinoline (homophthalimide dioxime) (4) (0.58 g, 60%), m.p. and mixed m.p. 223—225 °C (decomp.), *m/z* 191, and correct i.r. spectrum.[4] (ii) The chlorodicyanide (6) (1.32 g, 0.005 mol) in ethanol (50 ml) was treated as in (i) and the solution cooled to give the dioxime (4) (mixed m.p.; i.r.), a further crop of which (total 0.43 g, 45%) was obtained by evaporation of the filtrate, trituration of the residue with water, extraction of the mixture with ether (2 ×

10 ml), and filtration. The ether extract was dried ($MgSO_4$) and evaporated and the residue (0.45 g, 57%) crystallised from benzene–light petroleum (b.p. 60—80 °C) to yield yellow needles of *p*-chlorobenzaldehyde *anti*-oxime, m.p. 105 °C (lit.,[16] 106—107 °C), *m/z* 155. (iii) The dicyanide (1) (4.6 g, 0.02 mol) in ethanol (140 ml) was refluxed with hydroxylamine hydrochloride (5.56 g, 0.08 mol) and sodium hydrogen carbonate (6.72 g, 0.08 mol) in water (35 ml) for 27 h. Evaporation of the solution (to 0.5 vol) under reduced pressure and cooling gave *stilbene-*α,o-*bis(carboxamide oxime)* (5) (3.88 g, 66%) as prisms, decomp. at 230 °C (from ethanol–charcoal) (Found: C, 64.5; H, 5.4; N, 18.9. $C_{16}H_{16}N_4O_2$ requires C, 64.9; H, 5.4; N, 18.9%), *m/z* 296; $\lambda_{max.}$ (EtOH) 321 and 230 nm (ε × 10^{-3} 7, 13.2); $\nu_{max.}$ 3 420, 3 330, 3 245br, 1 675, 1 668, 1 640, 1 630, 1 575 cm^{-1}, *etc.* The bis(amide oxime) gave a violet colour with aqueous ethanolic iron(III) chloride. The bis(amide oxime) (0.5 g) in ethanol (150 ml) was heated under reflux with hydroxylamine hydrochloride (0.12 g) in water (10 ml) for 3 h. Evaporation of the solution to 40 ml and cooling gave homophthalimide dioxime (0.12 g), identified as before. (iv) The dicyanide (1) (2.3 g, 0.01 mol) in ethanol (70 ml) was refluxed with hydroxylamine hydrochloride (2.78 g, 0.04 mol) and sodium hydrogen carbonate (1.68 g, 0.02 mol) in water (35 ml) for 30 h. Evaporation under reduced pressure to half volume and cooling in ice gave 1-*hydroxyimino*-3-*oxo*-1,2,3,4-*tetrahydroisoquinoline* (8) (0.9 g, 51%) as flakes, decomp. 230 °C (from ethanol–charcoal) (Found: C, 61.1; H, 4.6; N, 15.8. $C_9H_8N_2O_2$ requires C, 61.4; H, 4.6; N, 15.9%), *m/z* 176; $\lambda_{max.}$ 220, 259, and 293 nm (ε × 10^{-3} 11.8, 9.0, and 1.5, respectively); $\nu_{max.}$ 3 200br, 1 665s, 1 644s, 1 582 cm^{-1}, *etc.* The monoxime (0.1 g) was refluxed in 3M-hydrochloric acid (30 ml) for 1 h and the solution cooled to give homophthalimide (0.065 g, 71%), identified by mixed m.p. and i.r. spectrum.[7]

(*c*) *With sodamide.* Sodamide (0.5 g) was cautiously dis-

1 380, 1 345s, 1 183 cm^{-1} (C–O) *etc.*; δ (CCl_4) 1.11 (t, Me, *J* 6.8 Hz), 1.92 (sextet, CH_2), 4.55 (t, OCH_2), and 7.2—8.3 (9 ring H); and sodium butoxide in butanol gave, after concentration of the reaction solution (to 15 ml) under reduced pressure, filtration, trituration of the tarry solid with ethanol, and recrystallisation (EtOH–charcoal), the 1-*butoxy derivative* (11; R = Bu, Ar = Ph) (12%) as needles, m.p. 108.5 °C (Found: C, 79.4; H, 6.1; N, 9.2. $C_{20}H_{18}N_2O$ requires C, 79.5; H, 6.0; N, 9.3%), *m/z* 302; $\nu_{max.}$ 2 230 (CN), 1 618, 1 580s, 1 558s, 1 510s, 1 430s, 1 358, 1 340s, 1 309w, 1 286w, 1 243w, 1 188 cm^{-1} (C–O), *etc.*; δ (CCl_4) 1.02 (*ca.* t, Me, *J* 6.8 Hz), 1.2—2.2 (c, CH_2CH_2), 4.61 (t, OCH_2, *J* 6.1 Hz), and 7.3—8.4 (9 ring H).

4-*Cyano*-3-*phenylisoquinolin*-1(2H)-*one* (12; Ar = Ph) *and Intermediates.*—(*a*) The 1-ethoxyisoquinoline (11; R = Et, Ar = Ph) (0.2 g) was refluxed in acetone (15 ml) with water (6.5 ml) and concentrated hydrochloric acid (4.5 ml) for 1 h, during which the product began to separate. Cooling the mixture in ice gave 4-cyano-3-phenylisoquinolin-1(2*H*)-one (12; Ar = Ph) (0.14 g, 78%), m.p. 270 °C (lit.,[10] 270 °C) (Found: C, 78.2; H, 4.2; N, 11.3. Calc. for $C_{16}H_{10}N_2O$: C, 78.1; H, 4.1; N, 11.4%); *m/z* 246; $\nu_{max.}$ 3 160br (bonded NH), 2 230 (CN), 1 665s (CO), 1 614, 1 500, 1 458s, 1 383, 1 347, 1 285w, 1 273w, 1 170w, 1 150, 884, 775w, 764, 701, and 690 cm^{-1}; $\lambda_{max.}$ 215, 233infl., 244infl., 310, 325sh and 340sh (ε × 10^{-3} 36.2, 19.3, 18.2, 15.8, 12.9, and 6.4 respectively); δ [$(CD_3)_2SO$] 7.3—8.0 (c, 8 ring H), 8.27 (dd, 8-H, *J* 7.2, 1.7 Hz), and 12.22br (NH). Similar acid hydrolysis of the 1-methoxyisoquinoline (11; R = Me, Ar = Ph) gave an identical product (m.p., i.r. spectrum).

(*b*) *o*-Cyanobenzyl cyanide was acylated[11] with benzoyl chloride in the presence of alkali to give an aqueous solution of the product enolate. (i) A portion, added to an excess of 3M-hydrochloric acid, provided 4-cyano-3-phenylisocoumarin (13)

crystals of a mixture A (0.75 g), found by ^{1}H n.m.r. to comprise 32% of the 1-methoxyisoquinoline (11; R = Me) and 68% of the dihydro analogue (15; R = Me). Fractional crystallisation of A (MeOH under N_2; 2nd crop) and recrystallisation (MeOH) yielded 4-*cyano*-3,4-*dihydro*-1-*methoxy*-3-*phenylisoquinoline* (0.15 g) as cubes, m.p. 122 °C (Found: C, 77.6; H, 5.3; N, 10.7. $C_{17}H_{14}N_2O$ requires C, 77.9; H, 5.3; N, 10.7%), *m/z* 262; $\nu_{max.}$ 2 250 (C≡N), 1 650s (C=N), 1 600, 1 580, 1 500, 1 450s, 1 355, 1 322, 1 319s, 1 300, 1 278, 1 198 (C–O), 1 145, 1 090, 1 050, 970, 869, 784, 755, 740, 700, 688, and 668 cm^{-1}; $\lambda_{max.}$ 211, 247, and 262sh nm ($\varepsilon \times 10^{-3}$ 26.5, 7.0, 4.4 respectively); δ ($CDCl_3$) 3.86 and 4.83 (d, d, 3-, 4-H, *J* 12 Hz), 3.88 (s, OMe), and 7.2—8.0 (c, 9 ring H); δ (C_6H_6) 3.30 and 4.44 (d, d, 3-, 4-H, *J* 13 Hz), and 3.61 (s, OMe).

(*b*) *Dehydrogenation.* (i) The mixture A in deuteriochloroform was unchanged (^{1}H n.m.r. after addition of $SiMe_4$) after being refluxed for 45 min with passage of oxygen. (ii) The pure dihydroisoquinoline solution from ^{1}H n.m.r. [in (*a*)] was evaporated, the residue taken up in methanol (1 ml), and fresh sodium methoxide (5 mg) added. With passage of oxygen, the solution was refluxed for 45 min. After evaporation and extraction of the residue into benzene, twice, the ^{1}H n.m.r. spectrum showed the presence of the 1-methoxyisoquinoline (11; R = Me, Ar = Ph), δ (C_6H_6) 3.60 (s, OMe), and of the 3,4-dihydro-1-methoxyisoquinoline (15; R = Me), δ 3.74 (s, OMe), in the molar ratio 47 : 53%. By evaporation and addition to the glassy residue of methanol (6 drops) crystals of the 1-methoxyisoquinoline (11; R = Me, Ar = Ph) were isolated (i.r. spectrum).

4-*Cyano*-1-*methoxy*-3-(4-*methoxyphenyl*)*isoquinoline* (11; R = Me, Ar = *p*-$MeOC_6H_4$).—*o*-Cyanobenzyl cyanide (10 g), (11; R = Me, Ar = Ph) from the filtrate; slight reduction in volume of the filtrate (reduced pressure) gave further crops. Compound (11; R = Me, Ar = Ph) formed needles (2.6 g, 25%) (from ethanol–charcoal), m.p. and mixed m.p. 152 °C, and i.r. spectrum as before. The main product, 1-*amino*-4-*cyano*-3-[2-(1-*cyano*-2-*phenylethenyl*)*phenyl*]*isoquinoline* (19; R = H) (4.85 g, 33%), crystallised from ethanol as prisms, m.p. 207 °C (Found: C, 80.3; H, 4.4; N, 15.1. $C_{25}H_{16}N_4$ requires C, 80.7; H, 4.3; N, 15.1%), *m/z* 372, $\lambda_{max.}$ 220, 255, 305, 344sh, and 360sh ($\varepsilon \times 10^{-3}$ 39.0, 26.2, 24.6, 12.0, and 6.4, respectively); $\nu_{max.}$ 3 485 and 3 368 (NH_2), 3 215 (bonded NH), 2 215 (αβ-unsaturated C≡N), 2 210 (C≡N conjugated to N), 1 630s, 1 617, 1 548, 1 508, 1 345, 1 152, 929, 874, 778, 769, 736, 691, and 682 cm^{-1}.

The powdered amine (3 g) was refluxed with acetic anhydride (20 ml) and acetic acid (20 ml) for 45 min, the hot solution poured onto ice (80 g), and the oil triturated to afford the 4-*acetamido derivative* (19; R = Ac) (2.4 g, 72%), m.p. 219 °C (from tetrahydrofuran) (Found: C, 78.0; H, 4.3; N, 13.6. $C_{27}H_{18}N_4O$ requires C, 78.3; H, 4.4; N, 13.5%), *m/z* 414; $\lambda_{max.}$ (tetrahydrofuran) 251, 305, 338sh and 352sh ($\varepsilon \times 10^{-3}$ 31.8, 25.2, 15.6, and 8.9 respectively); $\nu_{max.}$ 3 226 (NH), 2 223 (aryl CN), 2 213 (αβ-unsaturated CN), 1 685 (CO), 1 619, 1 601w, 1 576, 1 568, 1 510 cm^{-1}, *etc.*; δ[$(CD_3)_2SO$] 2.20 (s, Me), 7.2—8.2 (c, 13 H, ring and olefinic), 8.36 (*ca.* dd, 8-H, *J ca.* 8.5, 2 Hz), and 10.91 (br, NH, removed by D_2O).

Oxidative Degradations.—(*a*) The preceding acetamido derivative (19; R = Ac) (2.07 g, 0.005 mol) was dissolved in acetic acid (100 ml; AnalaR, glacial) and ozone (*ca.* 0.015 mol) was passed through at 10 °C during 30 min. Zinc dust (4 g) and water (100 ml) were added and the mixture was stirred for 2 h at 10 °C and then filtered. Addition of water (70 ml) and

solution of *o*-cyanobenzyl cyanide (2.2 g) in methanol (50 ml) mixed with sodium methoxide (0.1 g Na in 20 ml MeOH), kept at 60 °C. After 4 h, the solution was cooled in ice to give 4-cyano-1-methoxy-3-(4-methoxyphenyl)isoquinoline (1.65 g, 37%) as needles (from ethanol–charcoal), m.p. and mixed m.p. 168 °C, and i.r. spectrum as before. The reaction filtrate slowly deposited 1-*amino*-4-*cyano*-3-[2-(1-*cyano*-2-*phenylethenyl*)-4-*methoxyphenyl*]*isoquinoline* (1.62 g, 26%) as prisms (from tetrahydrofuran–ethanol–charcoal), m.p. 217 °C (Found: C, 77.6; H, 4.5; N, 14.0. $C_{26}H_{18}N_4O$ requires C, 77.6; H, 4.5; N, 14.0%), *m/z* 402; $\lambda_{max.}$ 219, 232infl., 256sh, and 325 nm ($\varepsilon \times 10^{-3}$ 44.8, 33.7, 23.8, and 32.2 respectively); $\nu_{max.}$ 3 497 and 3 301 (NH_2), 3 096 (bonded NH), 2 215 (αβ-unsaturated CN), 2 204 (CN conjugated to N), 1 645s, 1 604, 1 591, 1 577, 1 550, 1 512s, 1 430, 1 311, 1 255s (C–O), 1 180 cm^{-1}, *etc.*; δ ($CDCl_3$) 3.77 (s, OMe), 5.78 (br s, NH_2, removed by D_2O), 6.75—6.95 (*ca.* d, 2 H *ortho* to OMe), 7.16 (s, =CH–), and 7.4—8.1 (c, 10 ring H).

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